Annals of Medicine and Surgery 9 (2016) 61–66

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.annalsjournal.com

Attaining pathological complete regression for breast conservation – A pilot experience in a developing country

E.A. Sule [a, *], M.A. Nzegwu [b]

[a] Dept of Surgery, Delta State University Abraka, Delta, Nigeria
[b] Dept of Pathology, University of Nigeria Medical School, Nigeria

HIGHLIGHTS

- Extended chemotherapy sessions alongside re-excisions are successful in achieving much enhanced rates of pathologically complete remissions even for T3 tumours.
- Our findings shows a much higher PCR rates than previous studies on the subject.
- Neoadjuvant/adjuvant chemotherapy and serial re-excisions were utilized succesfully in attaining pathologically complete remission.
- The use of pathologically complete remissions as endpoints in breast conservation for breast cancer may be fraught with less controversy than negative margins.

ARTICLE INFO

Article history:
Received 29 March 2016
Received in revised form
31 May 2016
Accepted 31 May 2016

Keywords:
Cancer
Breast conservation
Pathologic complete remission(PCR)

ABSTRACT

Context: Local recurrence is a formidable risk consideration in employing breast conservation for breast cancer. However pathological complete regression (PCR) from chemotherapy has been associated with improved rates of recurrence. Lower PCR rates have been reported from earlier studies and our approach seeks to obtain higher PCR rates utilizing a two pronged approach of surgery and chemotherapy.
Objective: To determine success rates in attaining pathologically complete regression for breast conservation in non-metastatic breast cancer cases in a developing country and their clinical outcome.
Patients and methods: Patients diagnosed with early stage breast cancers had sequential anthracycline/taxane based neoadjuvant/adjuvant chemotherapy administered at three weekly intervals. Following an initial excision, re-excisions were done following three courses of doxorubicin based chemotherapy. Subsequent re-excisions in cases with failed complete pathological regression were repeated following additional three doxorubicin based chemotherapy cycles or at sequel third taxane based cycle. Endpoint was pathologically complete regression as determined on permanent sections.
Results: Patients ages ranged between 27 and 67 years, mean age 43years, SD 10.34 years, N = 20 Initial breast tumour sizes ranged between 0.5 and 9 cm, mean 4.05 cm, SD 2.38. There were three T4, four T3 tumours, seven T2 and six T1 tumours. Clinical axillary lymphadenopathy with pathological involvement was present in 11 cases. Histological diagnosis showed 13 cases of invasive ductal carcinoma (65.0%), 2 cases of ductal carcinoma insitu (10.0%), 1 papillary carcinoma (5.0%), 3 cases of invasive lobular carcinoma (15.0%) and non-specific type 1 (5.0%). Immunohistochemistry assessment available in 15 cases was positive for estrogen and progesterone receptors in 10 cases. Two cases (10.0%) exhibited 20% positivity for human epidermal growth factor receptor. Pathological complete regression (PCR) defined as no invasive or insitu tumour residuals in the excised tumour bed, was achieved in the 18 cases assessed. (100%) This was consistent with clinical complete response obtained. It was not determined in 2 cases though clinical complete response was obtained. PCR was determined in ten cases (50.0%) at the first reexcision, second reexcision in 4 cases (20.0%) and third reexcision in 4 cases (20.0%). Mean no of re-excisions 1.67 cm, SD 0.84. Six sequential anthracycline/taxane cycles were administered in 17 cases while three cases received anthracycline based chemotherapy only. Median duration of followup from diagnosis was 48 months ranging between 8 months and 144 months. There were two demises at 48 months and 36 months follow up.

* Corresponding author.
E-mail address: emmasule2010@gmail.com (E.A. Sule).

http://dx.doi.org/10.1016/j.amsu.2016.05.019

Conclusion: Extended chemotherapy sessions alongside re-excisions were successful in achieving much enhanced rates of pathologically complete remissions at 100% in this yet early report, thus improving breast conservation rates even for T3 and T4 tumours. Our study reports higher PCR rates.

1. Introduction

Conservative breast management (CBM) has become attractive for breast surgeons following the several large international trials showing equivalent survivals between mastectomy and conservative breast management for suitable cases [1–6]. This has taken several decades for acceptability, the first observation haven being made after Geoffrey Keanes reported equal outcomes following local tumour excision with radium irradiation to Halstead mastectomy in the early 20th century [7]. Being the standard of care for early breast cancer, the advantage of preserving the breast is balanced against the risk of local recurrence comparable to that from mastectomy. This is demonstrated with various series reporting similar recurrence rates for CBM and mastectomy at 10–20% of ipsilateral breast tumour recurrence (IBTR) or chest wall failure over 10 years [1,5]. While such local recurrences have been reported to be clinically isolated events in 75% of cases, they may herald the onset of distant metastases in up to 15% of cases [8]. Among the factors reported to promote local recurrence following breast conservation has been presence of residual tumour or incomplete pathological regression of tumour (positive margins of excision). Camp et al. [9] have shown that local recurrence depends on the status of the lumpectomy margin [10]. With local recurrence rates at 7% and 27% reported for negative and extensively positive margins respectively [11], achieving negative margins is extremely desirable if adequate local control rates must be attained in breast conservation.

Tumour negative margin describes an absence of tumour cells > 2 mm from the excised tumour margin. This has been bedeviled by controversy with various schools of thought concerning what constitutes the optimum margin. However, pathologically complete remission defined as absence of tumor residuals in breast and nodes, has been reported to be associated with favourable outcomes [12]. We believe that the use of pathologically complete remissions as endpoints in breast conservation for breast cancer may be fraught with less controversy than negative margins. It has been further enunciated that breast cancer patients who achieve pathological complete remission have an improved prognosis than their stage of disease. We think it to be a desirable endpoint in conservative breast management.

The bulk of literature on the subject has sought to employ the use of neoadjuvant chemotherapy only to achieve pathologically complete remission with varying degrees of success reported based on the hormonal and the HER 2neu receptor status [13]. One study reported a PCR rate at 11% [14]. Green et al. reported 28.2% and 15.7% PCR rates in their series for weekly and three weekly interval chemotherapy respectively [15]. We seek to employ neoadjuvant-adjuvant chemotherapy and surgery (excision) in achieving higher success rates as we perceive that the resultant lesser local tumour burden following surgery may enable earlier onset of PCR hence achieve complete remission even for tumours that may be perceived as having the least chance of PCR by older studies.

Determining pathological complete remission justifies the employment of breast conservation. However mastectomy is yet the treatment of choice and strong bias for breast surgeons in Nigeria, even in early cases [16]. Conserving breast surgery even though internationally acceptable still faces considerable hurdles to its implementation as the philosophy of 'more is better' still has an enormous following in Nigeria. Hoover et al. have stated in the United States that despite decades of work resulting in the declaration of conserving breast surgery at a National Institute of health Consensus development more than two decades ago as the treatment of choice for early breast cancer, there was an enormous disconnect on its utilization [17]. We are not aware of studies done in the West African subregion as breast conservation is regrettably at an infancy stage in the country and indeed the subregion. For breast conservation to gain popularity in the country, quality control measures must be set up, geared towards achieving local control rates comparable with mastectomy. It is our view that determining pathological complete remission employing a two pronged approach of excision and chemotherapy constitutes the avenue to achieve this. It is our conviction that higher success rates utilizing this approach may be achievable even for larger tumours.

2. Objective

To determine success rates at achieving pathological complete remission emanating from the employ of surgery (excisions) and chemotherapy in breast conservation for breast cancer.

3. Patients and methods

Patients presenting to the Author with a breast lump or mass from 2004 up to 2015 at the Central hospital Warri, Delta Nigeria and Curatio medicare Oncology clinics, Warri, Delta Nigeria were evaluated with history taking, general and systemic examination with emphasis on a clinical breast exam. Diagnosis of breast cancer was made following biopsy and histopathological confirmation by trained pathologist. Immunohistochemistry assessment was done with some of the samples. Staging was done with the benefit of mammogram, chest xray and abdominal ultrasound. Unavailability of technetium bone scan in the centre precluded its request. Those with early breast cancer were counselled on the surgical options of breast conservation and a total mastectomy. For breast conservation, gross excision of the tumour was done and specimens sent for histology. With adequacy of bone marrow function determined by a full blood count before chemotherapy cycles, doxorubicin and cyclophosphamide at three weekly intervals for 6 cycles was administered. Paclitaxel or docetaxel administered at three weekly intervals or weekly intervals was then administered sequentially. (AC/P) Further re-excisions of the tumour bed were timed between chemotherapy cycles to assess for pathologically complete remissions based on the clinical perception of response. Bone marrow function was assessed before each cycle and patients with white cell counts below 1,500 mm3 had granulocyte colony stimulating factor administered to booster counts. Pathologically complete remissions were defined histopathologically as no residual invasive or insitu tumour cells at tumour bed. Serial clinical breast exams were done during chemotherapy sessions to assess for clinical complete response. Clinical complete response was defined by no palpable breast lump or axillary lymph node, restoration of normal soft tissue consistency of the breast from earlier post surgical